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UNCERTAINTIES IN KINETIC HARD-MODELLING OF MULTIVARIATE SPECTROSCOPIC DATA

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INTRODUCTION

Kinetic hard-modelling of multivariate spectroscopic data is a well-established method for the determination of reaction mechanisms and associated rate constants [1]. It relies on a hard model defined by kinetic rate laws and requires the numerical integration of these rate laws in order to model the spectroscopic signal and to calculate the residuals which are minimised in the least squares sense by optimising the corresponding rate constants.

Uncertainties in experimental conditions, such as initial concentrations ($\sigma^2_{\mathbf{k},\mathbf{c_0}}$) or dosing rates ($\sigma^2_{\mathbf{k},\mathbf{f}}$) , are often neglected and thus errors in the fitted rate constants ($\sigma^2_{\mathbf{k}}$) estimated from the residuals only ($\sigma^2_{\mathbf{k},\mathbf{r}}$) typically tend to be underestimated compared to the ones resulting from multiple repetitions of the experiment under the same conditions.

In this work [2], we have incorporated these experimental uncertainties in initial concentrations and in dosing rates into the calculation of the errors in the fitted rate constants.

RESULTS: Simulated 3rd order reaction (*A*+*B*+*C*→*P*+*C*)

Our rigorous approach based on classical error propagation was validated with simulated data by a 'brute force' Monte-Carlo sampling. Rigorous error propagation required significantly less computation time compared to the Monte Carlo procedure (typically seconds compared to hours on a modern personal computer).

Table 1

Comparison of the fitted rate constant **k** and of the predicted uncertainty σ_k from error propagation with the values obtained by Monte-Carlo sampling (10 000 points). Numbers in brackets indicate the first insignificant digit.

	k [a]	σ_k [a]
Error propagation	1.75(2)·10^{-4}	± 0.02(2)·10^{-4}
Monte-Carlo	1.75(2)·10^{-4}	± 0.02(3)·10^{-4}

[a] in L^{2}mol^{-2}s^{-1}×10^{-4}

ERROR PROPAGATION

$$\sigma^2_{\mathbf{k}} = \mathrm{diag}\left(\mathbf{H}^{-1}\right)\sigma^2_{\mathbf{r}} + \mathrm{diag}\left(\left(\frac{\partial \mathbf{k}}{\partial \mathbf{c_0}}\right)^{\mathrm{T}} \mathrm{DIAG}\left(\sigma^2_{\mathbf{c_0}}\right)\left(\frac{\partial \mathbf{k}}{\partial \mathbf{c_0}}\right)\right) + \mathrm{diag}\left(\left(\frac{\partial \mathbf{k}}{\partial \mathbf{f}}\right)^{\mathrm{T}} \mathrm{DIAG}\left(\sigma^2_{\mathbf{f}}\right)\left(\frac{\partial \mathbf{k}}{\partial \mathbf{f}}\right)\right)$$

$$= \sigma^2_{\mathbf{k},\mathbf{r}} \qquad = \sigma^2_{\mathbf{k},\mathbf{c_0}} \qquad = \sigma^2_{\mathbf{k},\mathbf{f}}$$

RESULTS: Simulated 2nd order reaction (*A*+*B*→*P*)

Based on simulated data for a 2nd order rate law under batch conditions, the effect of the uncertainties in the initial reactant concentrations on the predicted error of the fitted rate constant was thoroughly investigated. It was shown that the predicted error in the fitted 2nd order rate constant is minimal when the reactants are mixed in exact stoichiometric amounts, or if the species with the lowest associated uncertainty in its initial concentration is in excess (pseudo-first order conditions).

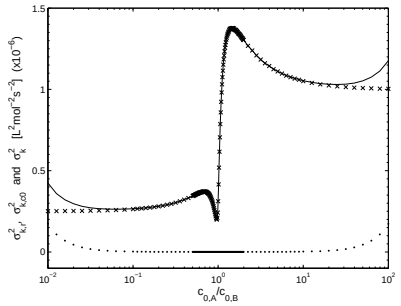


Figure 1

Individual contributions $\sigma^2_{k,r}$ (dotted line) and σ^2_{k,c_0} (crossed line) to the variance σ^2_k (full line) of the fitted rate constant **k** for the 2nd order reaction at various ratios $c_{0,A}/c_{0,B}$ of the initial concentrations ($c_{0,A}$+$c_{0,B}$=1 molL^{-1}) and imposed uncertainties of $\sigma_{c_{0,A}}$= 0.2%·$c_{0,A}$ and $\sigma_{c_{0,B}}$ = 0.1%·$c_{0,B}$.

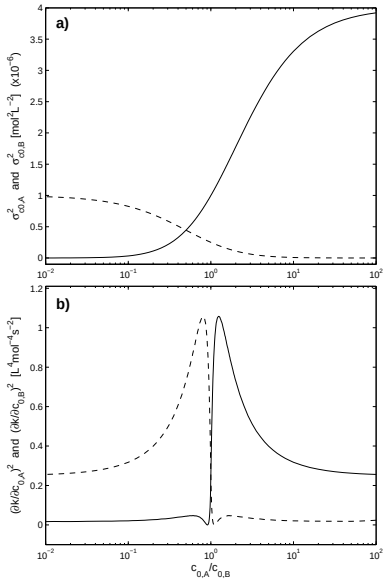
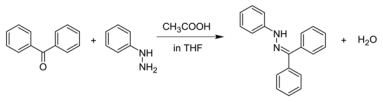


Figure 2

(a) Squared estimated uncertainties $\sigma^2_{c_0}$(full line for *A*, dashed line for *B*) in the initial concentrations and (b) squared derivatives of the fitted rate constant **k** with respect to the initial concentrations (full line: derivative with respect to *A*, dashed line: derivative with respect to *B*) for a 2nd order reaction at various ratios $c_{0,A}/c_{0,B}$ of the initial concentrations ($c_{0,A}$+$c_{0,B}$=1 molL^{-1}).

RESULTS: Experimental 3rd order reaction (*A*+*B*+*C*→*P*+*C*)

The reaction of benzophenone with phenylhydrazine was repeatedly (seventeen times) investigated by UV-vis and mid-IR spectroscopy under semi-batch conditions dosing the catalyst (acetic acid). Each measurement was analysed individually using a third order rate law and the standard deviation of each fitted rate constant was predicted by the proposed method of error propagation.



For UV-vis, each individual predicted standard deviation covered more than 80% of the experimental standard deviation over all individually fitted rate constants. For mid-IR, the prediction was only capable to explain approximately 40% of the experimental uncertainty in the fitted rate constant.

Possible reasons for this lower error predictability could be a larger sensitivity to temperature and/or stronger deviations from an assumed normally distributed and homoscedastic noise for mid-IR compared to UV-vis.

Amongst the individual contributions towards the predicted variance in the rate constant, the dosing rate has by far the largest impact (92%), followed by the initial concentrations (6%) and the variance due to the residuals (2%).

Table 2

Means of all individually fitted rate constants compared to their literature values obtained from UV-vis and mid-IR spectroscopy. Experimental standard deviations are compared to the mean uncertainties predicted by error propagation. Numbers in brackets indicate the first insignificant digit.

	UV-vis		mid-IR	
	k [a]	σ_k [a]	**k** [a]	σ_k [a]
Experimental	1.76(8)	0.02(8)	1.73(9)	0.05(4)
Error propagation	-	0.02(3)	-	0.02(2)
Literature	1.40 [b]	[c]	1.51 [b]	[c]

[a] in L^{2}mol^{-2}s^{-1}×10^{-4}
[b] for comparison, pseudo-second order rate constants of reference [3] have been recalculated to third order rate constants by division with the excess catalyst concentration given in [3]
[c] not available

CONCLUSIONS AND OUTLOOK

The possibility to reasonably predict the error in the rate constant based on one single multivariate kinetic measurement was demonstrated.

The proposed method of error propagation is simple to implement and fast to perform in order to receive a quick estimate of the error in the rate constant and the individual contributions to this error. It also allows to pinpoint the major source of error and to quantify their impact onto the fitted rate constant.

Furthermore, our approach can straightforwardly be extended to also cover other sources of uncertainty provided reasonable error estimates are available and can be propagated.

LIST OF SYMBOLS

H	(*nk* x *nk*)	Hessian matrix
k	(1 x *nk*)	Rate constants
$\mathbf{c_0}$	(1 x *nc*)	Initial concentrations
f	(1 x *nf*)	Dosing rates for the different dosing steps
$\sigma^2_{\mathbf{k}}$	(1 x *nk*)	Variances in the rate constants
$\sigma^2_{\mathbf{c_0}}$	(1 x *nk*)	Variances in the initial concentrations
$\sigma^2_{\mathbf{f}}$	(1 x *nk*)	Variances in the dosing rates
$\sigma^2_{\mathbf{k},\mathbf{r}}$	(1 x *nk*)	Variances of **k** due to the residuals
$\sigma^2_{\mathbf{k},\mathbf{c_0}}$	(1 x *nk*)	Variances of **k** due to the initial concentrations
$\sigma^2_{\mathbf{k},\mathbf{f}}$	(1 x *nk*)	Variances of **k** due to the dosing rates
diag	operator	Extraction of a diagonal vector from a matrix
DIAG	operator	Generation of a diagonal matrix from a vector
nc	scalar	Number of absorbing species
nk	scalar	Number of rate constants
nf	scalar	Number of different dosing steps
$\sigma^2_{\mathbf{r}}$	scalar	Variance of the residuals

CITED REFERENCES

[1] M. Maeder, Y.M. Neuhold, Practical Data Analysis in Chemistry, Elsevier, Amsterdam, NL, 2007.
[2] Billeter et al, Chemom. Intell. Lab. Syst. (2008), 93, 120-131.
[3] A.R. de Carvalho, M.D. Sanchez, J. Wattoom, R.G. Brereton, Talanta, 68 (2006), 1190-1200.